REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested.

Status of the Claims

Claims 5-18 and 23-32 were acted on by the Examiner in the Office Action dated March 31, 2005. A Reply under 37 C.F.R. § 1.116 to Final Office Action was filed on June 30, 2005, along with a Notice of Appeal. In response, an Advisory Action, dated September 19, 2005 was forwarded by the Examiner. Claims 5-18 and 23-32 have been rejected. The amendments to claims 7, 9, 10, 26 and 28 submitted with the Reply dated June 30, 2005 have not been entered. In response, applicants are submitting herewith a Request for Continued Examination.

Applicants respectfully request that the amendments submitted with the Reply dated June 30, 2005 not be entered. Instead, applicants request that the amendments submitted herewith be entered.

Claims 5-18 and 23-32 have been rejected. Claims 5-8 and 13-15 have been canceled. Claim 7 has been amended to correct the spelling of Creutzfeldt-Jacob syndrome. Claims 9 and 10 have been amended to correct the lack of antecedent basis for the term "pharmaceutical." Claim 26 has been amended to recite that the immunosuppressant is administered "in an amount such that the level of said transgenic product, as measured 15 days following the discontinuation of said administration of said immunosuppressant, is at least 50% greater than the level of said product when said immunosuppressant is not administered." Claim 28 has been amended to depend on Claim 26 rather than Claim 16. The amendments to Claims 7, 9, 10, and 28 are identical to the amendments submitted with applicants' Reply dated June 30, 2005. The amendment to Claim 26 was modified slightly for coherency. Accordingly, Claims 9-12, 16-18 and 23-32 are presented for examination.

A. Section 102(a) Rejections of Claims 26 and 27

Claims 26 and 27, directed to a method for increasing the tolerance of a mammal to transgenic cells, were rejected by the Examiner under 35 U.S.C. §102(a) as being anticipated by the disclosure of Smith et al., *Gene Therapy* (1996); 3:496-502 (Abstract only) (hereafter

"Smith et al.") and, alternatively, by the disclosure of Trapnell et al., International Publication No. WO 96/12406 (hereafter "Trapnell et al.").

Smith et al. (abstract only) is directed to a method of administering adenovirus vectors expressing a transgene along with administration of an immunosuppressant that will decrease the formation of anti-adenovirus neutralizing antibody to allow for a more effective second administration of an adenovirus vector.

Trapnell et al. is directed to a method of gene therapy involving the concurrent and repeated administration of a therapeutic gene of interest via an adenoviral vector and an immunosuppressive agent, such as DSG, for the suppression of the humoral immune response. Trapnell et al. is concerned with the repeated administration of an adenoviral vector and the resultant humoral immune response.

Claim 26 has been amended to recite that the immunosuppressant is administered "in an amount such that the level of said transgenic product, as measured 15 days following the discontinuation of said administration of said immunosuppressant, is at least 50% greater than the level of said product when said immunosuppressant is not administered." Claim 27 depends on Claim 26. Claim 28 has been amended to depend from Claim 26. Support for the amendment of Claim 26 can be found in Example 2, particularly Table 1 which compares, among other things, the levels of α1-antitrypsin of the control group (which received no immunosuppressant) and the DSG group (which received 5 days of DSG administration) for a period of 200 days following administration of the adenoviruses. Table 1 clearly shows the desired lasting effect of DSG on the expression of the transgenic product.

The Examiner has indicated in the Advisory Action dated September 19, 2005, that if the amendments, submitted with applicants' Reply dated June 30, 3005, had been entered, the amendments would have been sufficient to overcome this rejection. Because the amendment to Claim 26 submitted herewith is identical, except for a minor change to improve coherency, to the previously submitted amendment, applicants request that this rejection be withdrawn.

B. Double Patenting Rejection of Claim 25

The Examiner has asserted a statutory double patenting rejection of Claim 25 as being a substantial duplicate of Claim 28 and thus objectionable due to statutory type double patenting. Claims 25 and 28 previously both depended on Claim 16.

Claim 28 has been amended to depend from Claim 26. In light of applicants' amendment, the Examiner indicated in the Advisory Action that this double patenting rejection is no longer applicable and will be withdrawn.

C. Rejection of Claims 5 to18 and 23 to 32 Under 35 U.S.C. § 112, Second Paragraph

Claims 5-18 and 23-32 were rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner has maintained the rejection of Claim 16 as being vague and indefinite because it recites the term "the improvement" without antecedent basis for the term and because it is unclear to the Examiner how an improvement can comprise administration of an immunosuppressant. Claims 5-15, 17-18, 23-25, and 28 have been rejected because they depend on Claim 16. Claims 5-8 and 13-15 have been canceled. Claim 28 has since been amended to depend from Claim 26.

Applicants' Amendment of December 30, 2003 deleted the term "the improvement" from Claim 16. In the Advisory Action, the Examiner has indicated that this rejection will be withdrawn in light of applicants' remarks.

D. Rejections of Claims 5 to 18 and 23 to 32 Under the Enablement Requirement of 35 U.S.C. § 112, First Paragraph

Claims 5-18 and 23-32 were rejected by the Examiner under the enablement requirement of 35 U.S.C. §112, first paragraph. Claims 5-8 and 13-15 directed to a method of gene therapy have been canceled. Applicants respectfully traverse this rejection with respect to the remaining claims. Although the Examiner has very helpfully grouped the enablement issues into six categories, it is not always clear which categories apply to which claims. For purposes of this reply, Applicants will assume that the Examiner intended that each category be applied to each claim. Many of the claims, however, define subject matter that would render moot a particular enablement rejection.

Categories 1 and 5: As the Examiner has addressed categories 1 and 5 together,

Applicants will do the same. The Examiner has rejected the claims as lacking enablement for (1) "the administration of, or increasing the tolerance of, transgenic cells in any mammal including a man wherein the transgenic cells were from the same or different species[,] expressed any gene or where the method was for treating any disease by gene therapy or by *ex vivo* cell therapy" and (5) "the claimed method when transgenic cells are transplanted in a mammal or in a man, except for autologous cell transplantation which would produce minimal immune response."

Claim 16 is directed to "a method for expressing a transgenic product in a mammal comprising introducing into a cell of said mammal a transgene capable of expressing said transgenic product." Claims 9-12, 17-18, and 23-25 depend on Claim 16. Claim 29 contains the same recitation as Claim 16 namely that the transgene is introduced into "a cell of said mammal." Claims 30-32 depend on Claim 29. Accordingly these claims read only on transgenic cells derived from the same mammal in which they are transplanted.

Claim 26 is directed to transgenic cells that are produced "*in vivo* after the administration of a vector." Claims 27-28 depend on Claim 26. Since the transgenic cells are produced *in vivo* after the administration of the vector, the method involves only the cells from that particular mammal and does not involve cells from other species or *ex vivo* cell therapy.

In the Advisory Action dated September 19, 2005, the Examiner indicated that the Enablement rejection based on these issues would be withdrawn in light of applicants' remarks.

Category 2: The Examiner has rejected the claims as lacking enablement for "how transgenic cells would be prepared *in vitro* or how a transgenic cell would be administered to a mammal or what doses of the cell would be used." Applicants respectfully traverse this rejection.

With respect to Claim 16, the Examiner has recognized previously that this rejection does not apply. Claims 9-12, 17-18, and 23-25 depend on Claim 16. Claims 24 and 26 are directed to transgenic cells that are "produced *in vivo*." Claims 27-28 depend on Claim 26. Claim 29 is directed to "a method for increasing the tolerance of a mammal to transgenic cells comprising introducing into a cell of said mammal a transgene capable of expressing said transgenic product." Claims 30-32 depend on Claim 29.

In the Advisory Action dated September 19, 2005, the Examiner indicated that the Enablement rejection based on this issue would be withdrawn in light of applicants' remarks.

Category 3: The Examiner has withdrawn the rejection based on this issue.

Category 4: The Examiner has rejected the claims as lacking enablement for "how the methods of treatment of diabetes or AIDS, or DNA vaccination would be carried out, or what doses of the DSG would be used or what routes of administration would be used or which transgene would be used such that the effect of the transgene induced immune response is decreased by DSG treatment." Claims 5-8 and 13-15 directed to a gene therapy method have been canceled. Applicants respectfully traverse this rejection with respect to the remaining claims.

With respect to the issues regarding the treatment of particular diseases, Applicants address that issue with Category 6 below.

Claim 16 and dependent Claims 9-12, 17-18, and 23-25 are directed to "a method for expressing a transgenic product in a mammal." Claims 26 and 29 and dependent Claims 27-28, and 30-32 are directed to "a method for increasing the tolerance of a mammal to transgenic cells."

With respect to the routes of administration and the dosage of DSG covered by the claims, Applicants note that MPEP §2164.01 states that the test of enablement requires a determination as to whether one of skill in the art can practice the claimed invention without undue experimentation. Applicants note that such is the case. The claimed invention is a method for expressing a transgenic product in a mammal and a method for increasing the tolerance of a mammal to transgenic cells. One skilled in the art, seeking to practice such a method on a certain mammal containing a certain transgene can simply use the assay described on page 8 of the application to determine which immunosuppressant to use and in what amount, what route of administration to use, and how long such an immunosuppressant should be applied.

Moreover, the specification provides examples of administering the immunosuppressants, DSG, cyclosporin A, and FK 506, intraperitoneally, at given dosages, for various periods of time. In fact the claims, themselves, define what needs to be accomplished by one of skill in the art when choosing an immunosuppressant, a dosage, and

a route of administration. Whatever immunosuppressant, dosage, and route of administration is chosen, the administration of the immunosuppressant must result in a level of transgenic product, as measured 15 days following the discontinuation of the administration of the immunosuppressant, that is at least 50% greater than the level of the transgene product when the immunosuppressant is not administered. Thus, by routine experimentation, one of skill in the art by using the examples in the specification, the goal as set forth in the claims, and the knowledge in the art, would be able to determine a suitable combination of immunosuppressant, dosage, and route of administration to achieve the claimed level of transgenic product. Accordingly, practicing the claimed invention does not require undue experimentation.

As long as there is sufficient guidance to practice the claimed invention, Applicants are not required to submit information that can be determined by routine experimentation. As stated in the MPEP, section 2164.06:

> "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni,* 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" *In re Wands,* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt,* 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

Any experimentation necessary to determine an effective dosage or route of administration of an immunosuppressant would be routine for one skilled in the art in view of the more than reasonable guidance provided and the extensive guidance in the scientific literature on immunosuppressant administration. It cannot be the case that Applicants after discovering the lasting effects of immunosuppressant administration on the levels of transgenic products must provide examples of administering the immunosuppressant in different dosages and by different routes of administration. Such a requirement would be unduly burdensome on applicants and would be of little to no use to one of skill in the art. Accordingly, Applicants respectfully request that this rejection be withdrawn.

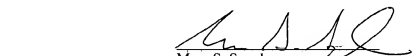
Category 6: The Examiner has rejected the claims as lacking enablement for "a method of gene therapy." Claims 5-8 and 13-15 directed to a method of gene therapy have

been canceled. Accordingly, this rejection is moot and should be withdrawn.

A favorable action on the merits is requested respectfully. A Petition for a two-month extension of time, from September 5, 2005 to November 5, 2005, is enclosed. The extension is measured from the date applicants' Appeal Brief was due, September 5, 2005, based on a Notice of Appeal received by the Patent Office on July 5, 2005.

The Commissioner is hereby authorized to charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 19-5425.

Respectfully submitted,



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